REMARKS

Claims 247-386 are pending in the application, and are subject to restriction in view of the Restriction Requirement mailed by the USPTO on October 14, 2009.

The Claim Amendments

The claims stand amended without acquiescence to any rejections and without prejudice to the prosecution of canceled subject matter in related divisional, continuation, and continuation-in-part applications.

The isolation of clones encoding **PRO224** is disclosed in the application at page 146, line 7 to page 147, line 11. The nucleic acid sequence of DNA33221-1133 is shown in Figure 1 (SEQ ID NO: 1) and the amino acid sequence of PRO224 derived from the coding sequence of SEQ ID NO: 1 is shown in Figure 2 (SEQ ID NO: 2) as disclosed at page 46, lines 13-16.

Applicants note that the phenotype of the knockout mice lacking expression of PRO224, comprised of physiological characteristics associated with disruption of the gene encoding PRO224, as disclosed in the application at page 162, line 19 to page 164 line 20, is described on page 164 lines 12-20 as follows: "by knocking out the gene identified as DNA33221-1133 encoding PRO224 polypeptides, both heterozygous and homozygous mutant progeny exhibit phenotypes which are associated with retinal degeneration. Such detected retinal changes are most commonly associated with cardiovascular systemic diseases or disorders that may be related to the vascular disease of hypertension (and any disease that causes hypertension, e.g. atherosclerosis), diabetes or other ocular diseases corresponding to ophthalmological disorders such as retinal degeneration. Thus, antagonists of PRO224 encoding genes would lead to similar pathological retinal changes, whereas agonists would be useful as therapeutic agents in the treatment of hypertension, atherosclerosis or other ophthalmological disorders including retinal degeneration and diseases associated with this condition (as indicated above)."

No new matter is added by way of the claim amendments.

The Restriction Requirement

The Examiner has required **restriction** between 39 groups of claims; each group of claims is subject to (A) a **further restriction** to a specific PRO molecule; and claims 249, 271, 273, 313, and 343 are (B) subject to a **yet further restriction** to a specific genus of diseases. In addition, some

claims are subject to **species election** regarding (i) neurological disorders, (ii) eye abnormalities, (iii) developmental abnormalities, (iv) cardiovascular, endothelial or angiogenic disorders, (v) immunological disorders, (vi) bone metabolic disorders, (vii) various physiological characteristics, and (viii) various behaviors.

In response to the requirements for restriction and election of species, Applicants select with traverse:

GROUP III **claims 272 – 291**

Directed to a method of identifying an agent that modulates a phenotype associated with a disruption of a gene

As directed to the specific PRO molecule:

PRO224 polypeptide **(encoded by DNA33221-1133 UNQ198)**

And as directed to the genus of diseases:

Eye abnormality

The USPTO has further required an election of species (pages 19-20 of the instant Office Action):

Applicants elect, with traverse, the following:

(ii) eye abnormalities (claims 256-262, 280-286, 320-326, and 356-362): retinal abnormality

(iv) cardiovascular, endothelial, or angiogenic disorders (claims 264, 288, 328, and 364): hypertension

(vii) physiological characteristics (claims 267, 291, 297, and 331): increased mean artery-to-vein ratio associated with retinal degeneration

Applicants believe that election of the species (i), (iii), (v), (vi), and (viii) are moot in view of the claim amendments.

Applicants Respectfully Traverse the Restriction Requirement

Applicants respectfully traverse the Restriction Requirement, for at least the reason that claims 272-291 (methods of identifying an agent that modulates a phenotype), 296, 297 (methods of identifying an agent that modulates a physiological characteristic), 313-331 (methods of identifying an agent that ameliorates or modulates a disorder or abnormality), and 342-343 (methods of evaluating a therapeutic agent) are all directed to subject matter related to the identification of agents that modify or affect the characteristics of animals having altered expression of particular polypeptides, which is recognized in the art as being similar and related subject matter, and for which a search would readily identify references related to the subject matter of all these claims.

In particular, these claims are all directed to subject matter related to phenotypes, which are comprised of physiological characteristics, and agents that act on such phenotypes, physiological characteristics, of the novel polypeptide termed PRO224; the claims are all related to a gene disruption of the gene that encodes for a PRO polypeptide; and all these claims share similar subject matter (e.g., disruption of the same gene; the phenotype comprised of the same physiological characteristics) that could be searched together, being related by gene and polypeptide sequences, and by the same identifying characteristics. Thus, a search for the subject matter of the elected Group III (claims 272 – 291) would necessarily also provide references related to the subject matter of other Groups, such as, for example, Group V (claims 296, 297), Group IX (claims 313-331), and Group XVI (claims 342, 343). Such a search for the subject matter of other groups, such as these other groups, which could be carried out along with the search for the elected Group III (claims 272 – 291), would not add to the search burden on the Examiner.

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **50-4634** (referencing Attorney's **Docket No. (123851-181879 (GNE-5201 R1))**.

Respectfully submitted,

Dated: October 30, 2009

By: _____
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